RELATIVE IMPORTANCE OF TRADITIONAL RISK FACTORS FOR MALIGNANT MELANOMA IN THE CZECH POPULATION

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SUMMARY

Aim: The Czech Republic is one of the leading European countries in incident cases of malignant melanoma (MM), which is on the rise. The study objective was to assess the strength of associations between MM and the known generally accepted risk factors for MM in the population of the Czech Republic.

Methods: The study was designed as a case-control study where cases were incident cases of MM detected at the Department of Dermatology and Venereology of the Bulovka Hospital. Controls were selected from cancer-free patients admitted to departments other than Dermatology and Venereology. Validated questionnaires were used to collect demographic, epidemiological, and clinical data.

Results: The binary logistic model shows the main risk factors for MM: male, female (OR = 0.292, 95% CI = 0.175–0.486), a changed mole (OR = 6.371, 95% CI = 3.774–10.756), a history of skin cancer (OR = 95.704, 95% CI = 37.241–10.756), and sunbeds use (OR = 3.594, 95% CI = 1.288–10.028). Using sunscreen products was considered as a protective factor against MM (OR = 0.253, 95% CI = 0.137–0.466).

Conclusion: The primary and secondary prevention increasingly emerges as a public health priority in the effort to reverse the negative trend in cases of MM and mortality from this disease in the Czech Republic. A prerequisite for an effective secondary prevention through screening is, among others, the identification of the population groups at highest risk for MM.

Key words: incidence, malignant melanoma, risk factors, screening, questionnaire, case-control study

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INTRODUCTION

The incidence of malignant melanoma (MM) is on the rise worldwide, with a 5% annual increase in patients newly diagnosed with melanoma. Melanoma is among the leading types of skin cancer. Unlike other skin cancers, it tends to metastasize rapidly to other organs. The most affected are the populations living in sunny countries such as New Zeland and Australia (1). The incidence of melanoma is higher in countries close to the Equator, but many cases also occur in Europe. The highest numbers of cases are reported in Switzerland, the Netherlands, Denmark, Norway, and Sweden (1–4). The prevalence of melanoma in the hispanic population of the USA is about six times lower than in the Caucasian population (4, 5). In the Afro-American population the prevalence is even twenty times lower (3). The epidemiological data show a constant 4–6% rise in incident cases of melanoma annually (6). In the Czech Republic, 2,044 cases of malignant melanoma (1,086 in males and 958 in females) were reported in 2011. Melanoma was the ninth most common cancer to be diagnosed in this country in 2012 (7, 8). The highest incidence of malignant melanoma in the years 2003–2011 in the Czech Republic was detected among men and women in Prague (9).

The increasing incidence of melanoma is often explained by improved diagnosis of early stages of this malignancy. Nevertheless, an expected proportional reduction in advanced stages of melanoma has not been observed and, therefore, the involvement of other factors should be considered. A possible explanation is low efficacy of melanoma screening in the Czech Republic, as it is not targeted at the population groups with the highest prevalence of melanoma.

The identification of the population group at the highest risk to be screened for melanoma should be based on the risk factors known to be associated with melanoma (10).

The highest number of both males and females diagnosed with melanoma are from the age group of 60–64 years (7). The most often reported risk factors for malignant melanoma are fair skin, fair hair and eyes, a family history of melanoma, immunosuppression, age, gender (females under 40 years of age and males over 40 years of age), multiple pigmented naevi, and excessive UV exposure (11–14).

As to the negative trend in melanoma, attention should be paid to the fact, among others, that the models derived from the observational epidemiological studies performed in the USA may not be generalizable to the European populations that are substantially more homogeneous than the American ones. In a homogeneous

population where the individuals are more similar to each other in terms of the distribution of the risk factors, particular risk factors may vary in weight from those in a population which is ethnically heterogeneous (14–16). A case-control study was initiated in 2011 to test the strength of associations between the generally recognized risk factors listed above and the incidence of MM in the Czech population. The aim was to obtain data specific for the Czech population for use in both the primary and secondary prevention of MM.

MATERIAL AND METHODS

The study was designed as a case-control study. The cases were incident, histologically confirmed cases, diagnosed at the Department of Dermatology and Venereology of the Na Bulovce Hospital (NBH) between June 2011 and December 2014.

Controls were selected from other departments of the same hospital to obtain a ratio of two age-matched controls per case. The control inclusion criteria were age ±3 years in comparison with the case and absence of other malignancy. No other selection criterion was used.

The presence of the risk factors in the study participants was determined by clinical examination by a dermatologist using a validated questionnaire developed by the Euromelanoma Task Force of the European Academy of Dermatology and Venereology. The questionnaire contains specific questions targeted at the markers of UV exposure (staying in a sunny country for more than or less than one year when aged under 18 years or over 18 years, number of days spent in a sunny country as an adult, using sunbeds, etc.), hereditary factors (a family history of skin cancer, fair hair and eyes, etc.), and using sunscreen products while tanning or while sun exposed during other activity (16).

For each risk factor or protective factor, the odds ratio (OR) and 95% confidence interval were calculated and differences in the distribution of the risk factors between cases and controls at the bivariate level were tested by the chi-square test. For multivariate analysis, binary logistic regression was applied. All studied variables were used to develop the model. The stepwise procedure was applied with probability for entry set at 0.005 and the probability for removal of variables from the model at 0.10. All tests were performed at a 5% level of significance.

Binary logistic model on the base of multivariate analysis shows that the main risk factors for malignant melanoma are: skin cancer history, changes in moles and sunbed use.

The IBM SPSS Statistics 20.0 software was used for analyses.

RESULTS

Within this study, 174 cases of MM were identified and paired with 345 controls. At the bivariate level, the controls did not differ significantly from the cases in terms of age (mean age of 59.9 and 58.3 years, respectively, p=0.282), education, a history of skin cancer in any relative, length of employment/outdoor employment, skin reactivity to solar radiation, getting severely sunburned at age under 18 years, staying in a sunny country, and using sunbeds (Table 1).

Table 1. *Bivariate analysis of the results – nonsignificant results*

Questionnaire item	OR	95% CI for OR		p value
		Lower bound	Upper bound	
Age (years)	1.006	0.995	1.017	0.282
Family history of skin cancer	0.582	0.165	2.055	0.401
Length of employment				0.199
1 year or less	2.037	0.645	6.433	0.225
1–5 years	0.891	0.358	2.217	0.804
6–10 years	0.157	0.020	1.210	0.076
10 years or more	1.405	0.767	2.574	0.271
Reactivity				0.126
Skin easy to get sunburned and difficult to get tanned	1.896	0.547	6.572	0.313
Skin first sunburned and then tanned	1.942	0.600	6.290	0.268
Skin sunburned a little and then tanned easily	1.290	0.401	4.145	0.669
Skin easy to tan	1.625	0.497	5.313	0.422
Not indicated	4.469	1.054	18.938	0.042
Severely sunburned skin when aged under 18 years				0.690
Yes	0.894	0.564	1.417	0.635
Do not remember	0.794	0.450	1.402	0.426
Staying in a sunny country:				0.324
Yes – when aged under 18 years	0.808	0.206	3.166	0.760
Yes – when aged over 18 years	0.471	0.174	1.279	0.140
Sunbed user – yes	1.290	0.547	3.041	0.561
Sunbed user – No. of years of sunbed use	0.989	0.881	1.111	0.858

Melanoma appeared to be statistically significantly associated with gender, with females being at lower risk of MM. At the bivariate level, MM was negatively associated with multiple pigmented naevi, skin cancer screening on request, using sunscreen products, and having a holiday in a sunny country. The results are summarized in Table 2.

Binary logistic model showed that at the level of multidimensional analysis, significant predictors of MM are variables concerning gender, changed mole, history of skin cancer, and sunscreen products and sunbeds use. The results are given in Table 3.

DISCUSSION

The aim of the study was to test the strength of associations between the generally recognized risk factors for MM (3, 10) and the incidence of this disease in the relatively highly homogeneous Czech Caucasian population as well as the usability of these factors to identify the population groups at highest risk for melanoma as target groups for screening. To collect data on exposure to risk factors, a validated questionnaire developed by the Euromelanoma Task Force of the European Academy of Dermatology and Venereology was used (17). In accordance with the initial assumption that the risk models derived from the experience of sunny countries with heterogeneous populations (18–22) may not be equally informative for the Czech population; at the bivariate level, no association was found between MM and some variables which are typical surrogate indicators of UV exposure such as length of outdoor employment (less than one year, 1–5 years, 5–10 years, or over 10 years), severe sunburn resulting in blisters at age under 18 years, long-term stay in a sunny country, or use of sunbeds. Neither was skin reactivity to solar radiation associated with MM in this study. In contrast to what is commonly believed, having a holiday in a sunny country appears to be a protective factor for MM, with an obvious biologi-

Table 2. *Bivariate analysis of results – significant results ($p < 0.05$)*

Questionnaire item	OR	95% CI for OR		p value
		Lower bound	Upper bound	
Gender: 1 for female	0.380	0.261	0.552	< 0.001
Multiple pigmented naevi	0.497	0.312	0.794	0.003
Changed mole	2.489	1.708	3.629	< 0.001
History of skin cancer	28.794	12.822	64.662	< 0.001
I want to get screened for skin cancer	0.068	0.040	0.117	< 0.001
Screened for skin cancer in the past	1.952	1.231	3.094	0.004
Sunscreen use while sun exposed more than hour				
Sometimes	0.333	0.207	0.534	< 0.001
Every time	0.597	0.347	1.027	0.063
I never sunbathe	1.127	0.591	2.149	0.716
Wearing sunscreen while sunbathing				
Sometimes	0.269	0.140	0.514	< 0.001
Every time	0.452	0.240	0.850	0.014
I never sunbathe	1.152	0.601	2.207	0.670
Number of weeks of summer holiday				
2 weeks or less	0.730	0.467	1.139	0.165
More than 2 weeks	0.332	0.194	0.569	< 0.001

Table 3. *Binary logistic model of associations between the incidence of suspected melanoma and risk factors in the participants of the European Day of Melanoma*

Simplest model	OR	95% CI for OR		p value
		Lower bound	Upper bound	
Gender: 1 for female	0.292	0.175	0.486	< 0.001
Changed mole	6.371	3.774	10.756	< 0.001
History of skin cancer	95.704	37.241	245.947	< 0.001
Using sunscreen while sun exposed for more than hour				
Sometimes	0.253	0.137	0.466	< 0.001
Every time	0.932	0.456	1.907	0.848
I never sunbathe	0.854	0.377	1.936	0.706
Sunbed user	3.594	1.288	10.028	0.015

cal gradient where the risk for MM decreases with an increasing length of the holiday in a sunny country. On the other hand, using sunscreen products significantly reduces the risk for MM and individuals having a longer holiday in a sunny country might be more likely to protect themselves better from UV radiation.

A possible explanation for some unexpected observations can be joint effects of two or more factors, e.g. using sunscreen products while sun exposed, getting screened for skin cancer on request, or having been screened for skin cancer in the past. It follows that the risk assessment at the bivariate level on basis of the questions of the validated questionnaire can be misleading either due to modifying or confounding effects.

The binary logistic model showed that if mutual effects of specific variables from the validated questionnaire are taken into account, the variables considered as surrogate indicators of UV exposure are reduced to the protective effect of sunscreen products and risk from sunbed use. Another risk factor for MM is a changed mole, which increases the risk for MM about six times. A history of skin cancer is an extremely high risk factor, with an OR of 95.70 (95% CI = 37.24–245.95). The last variable that had an effect on MM is gender, with females being at lower risk for MM than males. From the binary logistic model, it clearly follows that some of the bivariate relationships are confounded (e.g. using sunbeds is not a statistically significant risk factor at the bivariate level) and that only two (using sunscreen products and using sunbeds) of the external factors characterizing UV exposure are relevant, and possibly also differences in behavioural patterns between males and females.

CONCLUSION

Of the 17 factors presented in the validated questionnaire developed by the Euromelanoma Task Force of the European Academy of Dermatology and Venereology, only five were identified as significant predictors of MM. This finding supports scepticism about the generalizability of some MM risk models to a homogeneous Caucasian population. It is not a negative criticism, but rather an attempt to open the discussion about the need for adjusting them to the Central European conditions. Of the directly applicable results of the present study, the risk from using sunbeds needs to be underlined. In this regard, the prevention should target human behaviour. Similarly, using sunscreen products was found to be effective in protecting from MM.

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Conflict of Interests

None declared

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